

and insert the following therefor as a separate page after the claims:

Abstract of the Disclosure

a<sup>1</sup>  
Compounds are disclosed having the general formula  $R_1-X-R_2$ , wherein  $R_1$  and  $R_2$  are biologically active groups, at least one of which is polypeptidic. X is a non-peptidic polymeric group.  $R_1$  and  $R_2$  may be the same or different. Preferred  $R_1$  and  $R_2$  groups are TNF inhibitors.

In the Claims

Please delete claims 1-14 and 16-44, without prejudice or disclaimer.

Please amend claim 15, as follows:

a<sup>2</sup>  
15. A [substantially purified] compound of the formula  $R_1-X-R_2$ , wherein:

[X comprises a non-peptidic polymer having a first reactive group and a second reactive group, wherein said first reactive group is a Michael acceptor; and]

$R_1$  and  $R_2$  are each a tumor necrosis factor (TNF) inhibitor polypeptide selected from:

(a) 30 kDa TNF inhibitor or 40 kDa TNF inhibitor,

(b) 30 kDa TNF inhibitor or 40 kDa TNF inhibitor, modified to contain at least one non-native cysteine residue, and

(c) a biologically active portion of (a) or (b), wherein  $R_1$  and  $R_2$  bind to TNF; and

[comprises a biologically-active molecule having a reactive thiol moiety, said biologically-active molecule is covalently bonded to said non-peptidic polymer by reaction of said thiol moiety with said Michael acceptor, and said biologically-active molecule retains its biological activity after said reaction; and

$R_2$  comprises a biologically-active molecule or a nonbiologically-active group bonded to said non-peptidic polymer by reaction with said second reactive group]

X is a non-peptidic polymer having two activated groups linked thereto, said non-peptidic polymer being selected from polyethylene glycol, polypropylene glycol, polyoxyethylated glycerol and other polyoxyethylated polyols, polyvinyl alcohol and other polyalkylene oxides, polyoxyethylated sorbitol or polyoxyethylated glucose.

Please add the following new claims:

a<sup>3</sup>  
~~45~~<sup>47</sup>. The compound of claim ~~15~~<sup>15</sup>, wherein  $R_1$  and  $R_2$  are identical.

- 3  
46. The compound of claim ~~13~~<sup>1</sup>, wherein R<sub>1</sub> and R<sub>2</sub> are different.
- 4  
47. The compound of claim ~~13~~<sup>1</sup>, wherein R<sub>1</sub> and R<sub>2</sub> are said 30 kDa TNF inhibitor.
- 5  
48. The compound of claim ~~47~~<sup>4</sup>, wherein said 30 kDa TNF inhibitor is modified to contain at least one non-native cysteine residue.
- 6  
49. The compound of claim ~~48~~<sup>5</sup>, wherein said non-native cysteine residue is found at an amino acid residue site selected from the group consisting of 1, 14, 105, 111 and 165.
- 7  
50. The compound of claim ~~13~~<sup>1</sup>, wherein R<sub>1</sub> and R<sub>2</sub> are each a portion of said 30 kDa TNF inhibitor.
- 8  
51. The compound of claim ~~13~~<sup>1</sup>, wherein R<sub>1</sub> and R<sub>2</sub> are covalently bonded to X by thio-ether bonds.
- 9  
52. The compound of claim ~~51~~<sup>1</sup>, wherein cysteine residues of R<sub>1</sub> and R<sub>2</sub> are part of said thio-ether bonds.
- 10  
53. The compound of claim ~~13~~<sup>1</sup>, wherein R<sub>1</sub> and R<sub>2</sub> are attached to said polyethylene glycol via a cysteine residue.
- 11  
54. A pharmaceutical composition comprised of an effective amount of the compound of claim ~~13~~<sup>1</sup> in a pharmacologically acceptable carrier.
- 12  
55. The compound of claim ~~13~~<sup>1</sup>, which has been prepared by a method comprising simultaneously reacting R<sub>1</sub> and R<sub>2</sub> with X, wherein X has at least two reactive groups capable of forming thio-ether bonds when reacted with cysteine amino acid residues.
- 13  
56. The compound of claim ~~55~~<sup>12</sup>, wherein R<sub>1</sub> and R<sub>2</sub> are said 30 kDa TNF inhibitor or a portion thereof, modified to contain a non-native cysteine residue.
- 14  
57. The compound of claim ~~13~~<sup>12</sup>, which has been prepared by a method comprising reacting R<sub>1</sub> with X to form a complex R<sub>1</sub>-X and subsequently reacting said complex R<sub>1</sub>-X with R<sub>2</sub> to form the compound R<sub>1</sub>-X-R<sub>2</sub>, wherein X has at least two reactive groups capable of forming thio-ether bonds when reacted with cysteine amino acid residues.
- 15  
58. The compound of claim ~~57~~<sup>14</sup>, wherein R<sub>1</sub> and R<sub>2</sub> are said 30 kDa TNF inhibitor or a portion thereof, modified to contain a non-native cysteine residue.